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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,146	05/25/2001	Anthony E. Bolton	033136-182	8192

7590 12/23/2004

Gerald F. Swiss,
.Foley & Lardner LLP
Three Palo Alto Square
3000 El Camino Real Suite 100
Palo Alto, CA 94306-2121

EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)	
09/871,146	BOLTON ET AL.	
Examiner	**Art Unit**	
Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-19 and 33-52* is/are pending in the application.

4a) Of the above claim(s) *33-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-19 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 13, 2003 has been entered.

Response to Amendment

2. Claim 19 has been amended and claims 47-52 have been added as requested in the amendment filed on June 13, 2003. Claims 16-19 and 33-52 are pending in the instant application.

Claims 33-46 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 16-19 and 47-52 are under examination in the instant office action.

3. Applicant is reminded about the requirements of 37 CFR 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611,* Jun. 30, 2003) with respect to amendment to the claims.

4. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

6. Applicant's arguments filed on June 13, 2003 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 16-19 and 47-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for those reasons of record as applied to claim 19 in section 5 of Paper No. 8. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 17-18 are directed to pharmaceutical compositions comprising apoptotic bodies and claims 19 and 47-52 are directed to unit dosage compositions for administration to a human patient. Thus, the claimed invention is directed to means of "treatment and or prophylaxis of neurodegenerative and/or other neurological disorders by the administration of apoptotic cells and/or bodies" (page 5, lines 18-20 of the instant specification).

The nature of the invention is the demonstration that administration of suspended apoptotic bodies to mice under protocol of contact hypersensitivity , "an example of a Th-1-cell inflammatory disorder which is known to be mediated by inflammatory cytokines" (page 13, lines 5-6 of the instant specification), lead to "significant reduction in ear thickness (inflammation)" (page 14, line 21). Based on this single finding, Applicant concludes that "[t]he

effectiveness of the processes and compositions of the present invention in preventing and alleviating inflammation due to CHS indicates that administration of apoptotic cells and bodies as described up-regulates the *in vivo* generation of anti-inflammatory Th-2 derived cytokines such as IL-10". Applicant further hypothesizes that because "inflammatory cytokines are implicated in inflammation-related disorders of the brain, namely neuroinflammatory, neurodegenerative and neurological disorders" (second paragraph at page 16), then administration of apoptotic cells/bodies would lead to the treatment of these diseases.

As fully explained in the previous office action of record, neurological and neurodegenerative disorders represent vast number of conditions of different etiology, symptoms and development, ranging from trauma to genetic syndromes, for example Down's syndrome. While it is true that misbalanced levels of some inflammatory cytokines are characteristic for some of the neurodegenerative disorders, there is no evidence known at this moment or provided by the instant specification that would suggest that all neurological and neurodegenerative disorders can be associated with abnormal levels of inflammatory cytokines, absent evidence to the contrary. One skilled in the art would not have reasonable expectations that oral or intravenous administration of apoptotic bodies would lead to the treatment of a Down's syndrome patient, for example. There is also no basis for prophylaxis of Down's syndrome because it is a known genetic disorder characterized by abnormal triplication of 21st chromosome. Moreover, the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that a described model of contact hypersensitivity is adequate for study or treatment of neurodegenerative diseases in general. There is no indication in the prior art or the instant specification that would lead to a rational

suggestion to extrapolate the results of study of allergic contact dermatitis to the treatment of a neurodegenerative disorder, including disorders with shown cytokine misbalance.

While the skill level in the art is high, the level of predictability is low. While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the results contact hypersensitivity tests assessed on laboratory mice to other conditions, or to humans, in view of the absence of the art recognition that this model is suitable and predictable for any neurological or neurodegenerative disease, as implied by the instant specification.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:
"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed pharmaceutical or unit dosage compositions without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 16 is vague and indefinite for recitation of "an effective amount" without stating an objective as what the amount is effective for. Clarification is required.

10. Claim 17 recites the limitation "necrotic cells" in claim 16. There is insufficient antecedent basis for this limitation in the claim. Alternatively, it is not clear and cannot be determined from the claim or the instant specification how apoptotic bodies can comprise necrotic bodies. Clarification is required.

11. Claim 18 recites the limitation "liquid suspension of cellular material" in claim 16. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

December 22, 2004